Data for Brain Reference Architecture of YS24LongitudinallySegmentedDistalCA1andPeriphery

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Abstract

To support software development that mimics brain functions, datafication of the anatomical structure of neural circuits is being advanced in a standard format called Brain Information Flow (BIF). Uniform circuits are the minor descriptive units of the anatomical structure in BIF data. A uniform circuit consists of a group of neurons composed of specific cell types within a particular brain region, analogous to variables in software. To date, BIF data construction has been undertaken for various regions of the hippocampal formation, such as DG, CA3, CA2, CA1, S, PrS, PaS, MEC and LEC. However, considering the functional differentiation along the longitudinal and transverse axes, treating these as uniform circuits is too coarse-grained. Therefore, in this study, each brain region is treated as a uniform circuit, a decomposed area from the three-dimensional directions of the longitudinal, transverse and laminar organization, as finely as possible. Specifically, the longitudinal axis is divided into septal, intermediate and temporal types; the transverse axis into proximal and distal types; and for the laminar organization, based on a six-layer structure, the entorhinal cortex (EC) is further divided into three parts for the layer II and two parts for the layer V. The multiplication of the decomposed axes creates the refined uniform circuits. Next, using a mapping algorithm, the connections between brain regions within the hippocampal formation were analyzed based on the laminar organization and the divisions of the longitudinal and transverse axes, and this connection information was aggregated and listed. As a result, the detailed connection patterns of the hippocampal formation were determined. Notably, in this work, information processing experts were able to advance the construction of comprehensive data by extracting necessary information from neuroanatomy experts. .

Keywords: Brain Reference Architecture; Hippocampal formation; Longitudinal axis; Transverse axis

Author roles: Yudai Suzuki: Data curation, Methodology, Software, Writing – original draft; Yoshiko Honda: Investigation, Supervision, Validation,Writing – review and editing; Shinya Ohara: Investigation, Supervision, Validation, Writing – review and editing; Ayako Fukawa: Investigation,; Hiroshi Yamakawa: Conceptualization, Funding acquisition, Methodology,Project administration, Supervision,Visualization, Writing – review and editing

1 Overview

Repository location https://sites.google.com/wba-initiative.org/braes/data

Context This dataset was created as part of the activities of The Whole Brain Architecture Initiative (WBAI) to develop the Brain Reference Architecture (BRA). BRA is a project that aims to create a common reference architecture for the brain, which will serve as a foundation for reverse-engineering the brain and developing artificial general intelligence (AGI) (Yamakawa, 2021). The dataset focuses on the detailed anatomical connections within and around the hippocampal formation, which plays a crucial role in learning, memory, and spatial navigation.

The hippocampal formation consists of several regions, including the dentate gyrus (DG), CA3, CA2, CA1, subiculum (S), presubiculum (PrS), parasubiculum (PaS), medial entorhinal cortex (MEC), and lateral entorhinal cortex (LEC). These regions are known to exhibit functional differentiation along the longitudinal axis (septal, intermediate, temporal), transverse axis (proximal, distal), and laminar organization (layers 1-6) (Fanselow & Dong, 2010; Lee, GoodSmith, & Knierim, 2020; Ohara et al., 2023).

To create a comprehensive and standardized dataset of the hippocampal formation's anatomical connections, we applied the structure-constrained interface decomposition (SCID) method proposed by Yamakawa (2021). This method allows for the systematic decomposition of brain regions into smaller functional units called "uniform circuits" and the mapping of their connections based on anatomical and physiological evidence.

The resulting dataset, named "YS24LongitudinallySegmentedDistalCA1andPeriphery," provides a detailed and standardized representation of the hippocampal formation's anatomical connections in the Brain Information Flow (BIF) format. This dataset can be used for various purposes, such as understanding the structure-function relationships in the hippocampus, elucidating the mechanisms of brain disorders involving the hippocampus, and developing computational models of hippocampal function.

The dataset is made publicly available through the Brain Reference Architecture Editorial System (BRAES) to facilitate collaboration and data sharing among researchers in neuroscience, artificial intelligence, and related fields.

Table 1: Abbreviation and official name of the region of the hippocampal formation treated in this research

abbreviated name	formal name
DG	dentate area (dentate gyrus)
CA3	CA3 region of Hipp
CA1	CA1 region of Hipp
S	sub
LEC	lateral (anterior) entorhinal cortex

Table 2: Abbreviation and official name of the longitudinal axis classification treated in this research

abbreviated name	formal name
s	septal
i	intermediate
t	temporal

Table 3: Abbreviations and formal names of the transverse axes classifications treated in this research

abbreviated name	formal name
p	proximal
d	distal

Table 4: Abbreviations and formal names of laminar organization treated in this research

abbreviated name	formal name
L1	layer 1
L2_3	layer 2&3
L2	layer 2
L2fan	fan cells in layer 2
L3	layer 3
L5_6	layer 5&6
L5	layer 5
L5a	layer 5a
L5b	layer 5b
L6	layer 6

We created BIF information based on multiple detailed documents related to the anatomy around the hippocampal formation. In this study, there were five regions of the hippocampal formation (DG, CA3, CA1, S, and LEC), and four of them were ROIs (DG, CA3, CA1, S). Table 1 shows the abbreviations and formal names of the regions of the hippocampal formation that are treated in this study. The hippocampal formation was divided into three axes: longitudinal axis, transverse axis, and laminar organization. Tables 2, 3, and 4 show abbreviations, and formal names for the classification of the longitudinal axis, transverse axis, and laminar organization that are treated in this study.

The circuits were developed using the section "Circuit formulation". A total of 145 circuits were developed. The connections were developed using the section "Connection formulation". A total of 183 connections were established.

2 Method

SCID method/Function-oriented SCID method The series of procedures followed to produce the dataset according to structure-constrained interface decomposition (SCID) method (Yamakawa, 2021) or function-oriented SCID method (Yamakawa et al., 2023).

The brief introduction of three steps of SCID method is given as follows:

Step 1. Brain Information Flow (BIF) registering and provisonary creation of Hypothetical Component Diagram. This steps include (a) surveying anatomical knowledge in specific brain region (ROI: region of interest), (b) following determination of ROI and TLF (top-level function) consistently and (c) creation of a provisionary component diagram (called HCD)

Step 2. Enumerating candidate component diagram.

Step 3. Rejecting diagram that are inconsistent with scientific knowledge.

You can see more details about these steps in (Yamakawa, 2021).

Sampling strategy The dataset was created by the authors, including experts in anatomy, through the collection and integration of data from multiple publications. The selection criteria for the referenced publications were based on their inclusion in major academic journals related to anatomy. Detailed information about the referenced publications, such as titles, authors, journals, and publication years, is provided in the "References" sheet of the dataset.

The documents covered this time are as follows. Bienkowski et al. (2018); Dolorfo and Amaral (1998); Fanselow and Dong (2010); Honda and Ishizuka (2015); Honda and Shibata (2017); Lee, GoodSmith, and Knierim (2020); Ohara et al. (2021, 2023); Taniguchi, Fukawa, and Yamakawa (2022); Witter (2007)

Examination of correspondence of connections in longitudinal axis Fanselow and Dong (2010) divides the longitudinal axis of the hippocampus into three parts: septal, which is involved in cognitive processes related to learning, spatial memory, exploration, and movement; intermediate, which is involved in converting cognitive and spatial information into motivation and survival behavior; and temporal, which is related to motivational and emotional behavior. Therefore, the direction of the longitudinal axis was divided into three: septal, intermediate, and temporal.

Next, we investigated the correspondence between longitudinal axis connections in the hippocampal formation.

- In Honda and Shibata (2017), the following connections are said to have a projection relationship:
  - CA1→S: CA1_s projects to S_s, CA1_i projects to S_i, and CA1_t projects to S_t.
  - S→PrS: S_s projects to PrS_s, S_i projects to PrS_i, and S_t projects to PrS_t.
  - PrS→MEC: PrS_s projects to MEC_s, PrS_i projects to MEC_i, and PrS_t projects to MEC_t.
  - MEC→PrS: MEC_s projects to PrS_s, MEC_i projects to PrS_i, and MEC_t projects to PrS_t.
  - MEC→CA1: MEC_s projects to CA1_s, MEC_i projects to CA1_i, and MEC_t projects to CA1_t.
- In Honda and Ishizuka (2015), the following connections are said to have a projection relationship:
  - S→PrS: S_s projects to PrS_s, S_i projects to PrS_i, and S_t projects to PrS_t.
  - S→PaS: S_s projects to PaS_s, S_i projects to PaS_i, and S_t projects to PaS_t.
  - S→MEC: S_s projects to MEC_s, S_i projects to MEC_i, and S_t projects to MEC_t.
  - S→LEC: S_s projects to LEC_s, S_i projects to LEC_i, and S_t projects to LEC_t.
- In Bienkowski et al. (2018), the following connections are said to have a projection relationship:
  - DG→CA3: DG_s projects to CA3_s, DG_i projects to CA3_i, and DG_t projects to CA3_t.
  - CA3→CA1: CA3_s projects to CA1_s, CA3_i projects to CA1_i, and CA3_t projects to CA1_t.
  - CA1→S: CA1_s projects to S_s, CA1_i projects to S_i, and CA1_t projects to S_t.
- In Dolorfo and Amaral (1998), the following connections are said to have a projection relationship:
  - MEC→DG: MEC_s projects to DG_s, MEC_i projects to DG_i, and MEC_t projects to DG_t.
  - LEC→DG: LEC_s projects to DG_s, LEC_i projects to DG_i, and LEC_t projects to DG_t.

Based on these findings, we hypothesized that for the eight regions of the hippocampal formation (DG, CA3, CA1, S, PrS, PaS, MEC, and LEC), longitudinal axis connections would have a correspondence relationship even for connections other than those mentioned in the above literature. In the longitudinal axis, three hypotheses are established:

1. The first hypothesis is established that if the connection of two regions exists, DG_s, CA3_s, CA1_s, S_s, PrS_s, PaS_s, MEC_s, LEC_s have a correspondence relationship of the connection.
2. The second hypothesis is established that if the connection of two regions exists, DG_i, CA3_i, CA1_i, S_i, PrS_i, PaS_i, MEC_i, LEC_i have a correspondence relationship of the connection.
3. The third hypothesis is established that if the connection of two regions exists, DG_t, CA3_t, CA1_t, S_t, PrS_t, PaS_t, MEC_t, LEC_t have a correspondence relationship of the connection.

The above research findings and hypotheses were collected for each pair of source region and target region, and a list of information regarding the correspondence of connections in longitudinal axis was created.

Examination of correspondence of connections in transverse axes In Lee et al. (2020) the transverse axis of the hippocampus is divided into two parts: LEC, CA1_distal, and S_proximal are related to the self-centered coordinate system, and MEC, CA1_proximal, and S_distal are related to the environment-centered coordinate system. It states a hypothesis regarding functional differences. Therefore, the direction of the transverse axis was divided into two: proximal and distal.

Next, we examined the correspondence of connections between the transverse axes of the hippocampal formation region.

- In Honda and Shibata (2017), the following connections are said to have a projection relationship:
  - CA1→S: CA1_d projects to S_p.
  - PrS→MEC: PrS_d projects to MEC_p.
  - MEC→PrS: MEC_p projects to PrS_d.
- In Honda and Ishizuka (2015), the following connections are said to have a projection relationship:
  - S→PrS: S_d projects to PrS_d, and S_d projects to PrS_p.
  - S→MEC: S_d projects to MEC_d, and S_d projects to MEC_p.
  - S→LEC: S_p projects to LEC_d, and S_p projects to LEC_p.
- In Lee et al. (2020), the following connections are said to have a projection relationship:
  - LEC→CA1: LEC_d projects to CA1_d, and LEC_p projects to CA1_d.
  - MEC→CA1: MEC_d projects to CA1_p, and MEC_p projects to CA1_p.
  - CA1→S: CA1_d projects to S_p, and CA1_p projects to S_d.
  - S→LEC: S_p projects to LEC_d, and S_p projects to LEC_p.
  - S→MEC: S_d projects to MEC_d, and S_d projects to MEC_p.

Based on these findings, we hypothesized that the connections in the transverse axis of the five regions of the hippocampal formation (CA1, S, PrS, MEC, and LEC) have a corresponding relationship with respect to connections between regions other than those mentioned in the above literature. In the transverse axis, four hypotheses are established.

1. The first hypothesis is established that if the connection of two regions exists, CA1_d, S_p, LEC_d have a correspondence relationship of the connection.
2. The second hypothesis is established that if the connection of two regions exists, CA1_d, S_p, LEC_p have a correspondence relationship of the connection.
3. The third hypothesis is established that if the connection of two regions exists, CA1_p, S_d, PrS_p, MEC_d have a correspondence relationship of the connection.
4. The fourth hypothesis is established that if the connection of two regions exists, CA1_p, S_d, PrS_d, MEC_p have a correspondence relationship of the connection.

In addition, the correspondence relationship between the connections of the transverse axes regarding the two regions of the hippocampal formation (DG, CA3) is described in Lee et al. (2020).

- In Lee et al. (2020), the following connections are said to have a projection relationship:
  - DG→CA3: DG projects to CA3_p, and DG projects to CA3_d.
  - CA3→DG: CA3_p projects to DG.

- MEC→CA3: MEC_d projects to CA3_d, MEC_d projects to CA3_p, MEC_p projects to CA3_d, and MEC_p projects to CA3_p.
- LEC→CA3: LEC_d projects to CA3_d, LEC_d projects to CA3_p, LEC_p projects to CA3_d, and LEC_p projects to CA3_p.
- CA3→CA1: CA3_d projects to CA1_p, and CA3_p projects to CA1_d.

The above research findings and hypotheses were collected for each pair of source region and target region, and a list of information regarding the correspondence of connections in transverse axes was created.

Examination of the correspondence of connections in laminar organization The literature on the correspondence of connections in laminar organization is in Honda and Shibata (2017), Ohara et al. (2023), Ohara et al. (2021), Taniguchi et al. (2022).The above research findings were collected for each pair of source region and target region, and a list of information regarding the correspondence of connections in laminar organization was created.

Regarding the classification of laminar organization, the laminar organization of five regions of the hippocampal formation (DG, CA3, CA1, S, and LEC) were extracted from an Allen Brain Reference Atlas (n.d.). At this time, after discussions with experts, it was decided not to deal with LEC_3a and LEC_3b. Furthermore, Honda and Shibata (2017) describes the connections related to LEC_L2_3 and LEC_L5_6, so these were extracted as laminar organization. Furthermore, from Ohara et al. (2021), LEC_L2fan, LEC_L5a, and LEC_L5b were extracted as laminar organization.

Determining ROI and axis classification In this study, there were five regions of the hippocampal formation (DG, CA3, CA1, S, and LEC), and four of them were ROIs (DG, CA3, CA1, S) (Table 1). We determined the classification of the longitudinal axis, transverse axis, and laminar organization to be treated in this study (Tables 2, 3, and 4).

Based on the studies in the sections "Examination of correspondence of connections in longitudinal axis", "Examination of correspondence of connections in transverse axes", and "Examination of the correspondence of connections in laminar organization", for each region of the hippocampal formation treated in this study, the elements with the smallest grain size in each direction of the longitudinal axis, transverse axis, and laminar organization were extracted, and these were used as elements for dividing each direction of the longitudinal axis, transverse axis, and laminar organization. Table 5 shows the elements that divide the longitudinal axis, transverse axis, and laminar organization in the region of the hippocampal formation. Based on discussions with experts, it was decided not to determine the elements to be divided in the laminar organization of CA1, CA3, DG, and S, and in the transverse axis of DG.

Table 5: Elements that divide the longitudinal axis, transverse axis, and laminar organization regarding the region of the hippocampal formation

Region name	longitudinal axis	transverse axis	laminar organization
CA1	Septal,Mid,Temporal	Proximal,Distal	
CA3	Septal,Mid,Temporal	Proximal,Distal	
DG	Septal,Mid,Temporal		
S	Septal,Mid,Temporal	Proximal,Distal	
LEC	Septal,Mid,Temporal	Proximal,Distal	1,2_fan,3,5a,5b,6

Circuit formulation The naming convention for region abbreviations was as follows:

- "abbreviation of region name"_"s/i/t"_"p/d"."abbreviation of laminar organization"

The naming convention for the formal names of regions was as follows:

- "formal name of laminar organization" "of" "septal/intermediate/temporal" "proximal/distal" "formal name of region name"

A circuit was created by using the algorithm Make_Circuit. For each of the five regions of the hippocampal formation (DG, CA3, CA1, S, LEC), the following circuits were registered:

- "abbreviation of region name" _"s/i/t"
- "abbreviation of region name" _"p/d"
- "abbreviation of region name"_."abbreviation of laminar organization"

Then, by multiplying the elements that divide the longitudinal axis, transverse axis, and laminar organization directions by the three axes, the following circuits around the hippocampus were created and registered as a uniform circuit:

- "abbreviation of region name"_"s/i/t"_"p/d"."abbreviation of laminar organization"

Algorithm 1 Algorithm for creating a circuit: Make_Circuit
For DG, only line 3-5 are executed, with uniform circuit=True
For CA3, CA1, and S, line 9 and 14 are not executed
For LEC, "i_j.l" is appended in line 10-21, because connection to DG as "i_j" exists

```
1: List=[]
2: for extract element i from region name in Table 5 do
3:   for extract element j from longitudinal axis in Table 5 do
4:     append "i_j" to List as uniform circuit = False
5:   end for
6:   for extract element k from transverse axis in Table 5 do
7:     append "i_k" to List as uniform circuit = False
8:   end for
9:   for extract element l fromlaminar organization in Table 5 do
10:    append "i_l" to List as uniform circuit = False
11:  end for
12:  for extract element j from longitudinal axis in Table 5 do
13:    for extract element k from transverse axis in Table 5 do
14:      for extract element l fromlaminar organization in Table 5 do
15:        append "i_j_k.l" to List as uniform circuit = True
16:      end for
17:    end for
18:  end for
19:  if there is an exception then
20:    append the exception to List
21:  end if
22: end for
23: return List
```

Connection formulation A Connection was created using the algorithm Make_Connection. Using "a list of information regarding the correspondence of connections in longitudinal axis", "a list of information regarding the correspondence of connections in transverse axes", and "a list of information regarding the correspondence of connections in laminar organization", connections were created. For each of the five regions of the hippocampal formation (DG, CA3, CA1, S, LEC), if there is a connection from one region to another region, the following connections were registered:

- "a connection from one region to another region"
- "a connection from one region to another region considering a list of information regarding the correspondence of connections in longitudinal axis"
- "a connection from one region to another region considering a list of information regarding the correspondence of connections in transverse axes"
- "a connection from one region to another region considering a list of information regarding the correspondence of connections in laminar organization"

Using the mapping algorithm Synthesize_process, we analyzed the connections related to each region of the hippocampal formation treated in this study based on the longitudinal axis, transverse axis, and laminar organization, and compiled this connection information into a list. In the mapping algorithm, the individual correspondence of connections for each region of the hippocampal formation is developed in three dimensions: correspondence of longitudinal axis connections, correspondence of connections of transverse axis, and correspondence of connections of laminar organization. From the results of Synthesize_process, the following connections were registered:

- "a connection from one region to another region considering a list of information regarding the correspondence of connections in longitudinal axis, transverse axes, and laminar organization"

3 Dataset Description

Repository name BRA Editorial System (BRAES).

Object name YS24LongitudinallySegmentedDistalCA1andPeriphery.bra and YS24LongitudinallySegmentedDistalCA1andPeri

Algorithm 2 Synthesize_process (i1–i2, j1–j2, k1–k2, l1–l2)
For DG, line 2-3 are not executed
For CA3, CA1, and S, line 3 is not executed

```
1: for extract source j1 and target j2 from a list of information regarding the correspondence of connections in longitudinal axis do
2:   for extract source k1 and target k2 from a list of information regarding the correspondence of connections in transverse axes do
3:     for extract source l1 and target l2 from a list of information regarding the correspondence of connections in laminar organization do
4:       append "from i1_j1_k1.l1 to i2_j2_k2.l2" to List
5:     end for
6:   end for
7: end for
8: return
```

Format names and versions Template-v2-0.bra, XML

Creation dates 2022-09-11 : 2024-06-Unknown
The start and end dates of when the data was created (YYYY-MM-DD).

Dataset creators Please list anyone who helped to create the dataset (who may or may not be an author of the data paper), including their roles (using and affiliations).

Language English.

License The open license under which the data has been deposited (CC-BY 4.0).

Publication date 2024-06-16.

4 Reuse Potential

The Brain Reference Architecture (BRA) data, including standardized Brain Information Flow (BIF) data, has significant reuse potential for researchers within and beyond neuroscience. Its standardized nature allows for easy integration of mesoscopic brain information, enabling comparative analyses across brain regions. The data's versatility supports various research areas, including understanding brain structure-function relationships, elucidating brain disorder mechanisms, and constructing computational models.

This data contains hypotheses, so care must be taken when using it. The connection data with source_uc is a temporary circuit required when executing the algorithm Make_Connection, so care must be taken when using it. Future challenges include adding CA2, PaS, PrS, and MEC, and adding external connections other than the hippocampal formation.

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Competing interests

The author(s) has/have no competing interests to declare.

Algorithm 3 Algorithm for creating a connection: Make_Connection
For DG, line 7 and 14 are not executed
For CA3, CA1, and S, line 10 and 15 is not executed
In line 24, about the internal connections of the DG, CA3, CA1, and S, the widely known connections in Bienkowski et al. (2018) were extracted through discussion with experts.
In line 25, in some connections, if the source in ROI is not Uniform Circuit, add "Source _uc" to the Circuit and change the Connection Source to "Source _uc".

```
1: List=[]
2: for extract source i1 and target i2 from a list of information regarding the correspondence of connections in laminar organization do
3:   append "from i1 to i2" to List
4:   for extract source j1 and target j2 from a list of information regarding the correspondence of connections in longitudinal axis do
5:     append "from i1_j1 to i2_j2" to List
6:   end for
7:   for extract source k1 and target k2 from a list of information regarding the correspondence of connections in transverse axes do
8:     append "from i1_k1 to i2_k2" to List
9:   end for
10:  for extract source l1 and target l2 from a list of information regarding the correspondence of connections in laminar organization do
11:    append "from i1.l1 to i2.l2" to List
12:  end for
13:  for extract source j1 and target j2 from a list of information regarding the correspondence of connections in longitudinal axis do
14:    for extract source k1 and target k2 from a list of information regarding the correspondence of connections in transverse axes do
15:      for extract source l1 and target l2 from a list of information regarding the correspondence of connections in laminar organization do
16:        Synthesize_process (i1–i2, j1–j2, k1–k2, l1–l2)
17:      end for
18:    end for
19:  end for
20:  if there is an exception then
21:    append the exception to List
22:  end if
23: end for
24: append internal connections to List
25: if there is an exception then
26:   append the exception to List of circuits and List of connections
27: end if
28: return List
```

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